Atty. Dkt. No. SALK3140US-1
(088802-9803)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants Downes et al.

Title: STRUCTURE OF THE FARNESOID X RECEPTOR LIGAND BINDING DOMAIN AND METHODS OF USE THEREFOR

Appl. No.: 10/535,042

Filing Date: 05/13/2005

Examiner: Not yet assigned

Art Unit: 1646

Conf. No. 2218

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Stephen E. Reiter
(Printed Name)

(Signature)

March 27, 2006
(Date of Deposit)

INFORMATION DISCLOSURE STATEMENT UNDER 37 CFR §1.56

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Submitted herewith on Form PTO/SB/08 is a listing of documents known to Applicants in order to comply with Applicants' duty of disclosure pursuant to 37 CFR §1.56.

A copy of each non-U.S. patent document and each non-patent document is being submitted to comply with the provisions of 37 CFR §1.97 and §1.98.

The submission of any document herewith, which is not a statutory bar, is not intended as an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR

§1.56(b). Applicants do not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document which is determined to be a *prima facie* art reference against the claims of the present application.

TIMING OF THE DISCLOSURE

The listed documents are being submitted in compliance with 37 CFR §1.97(b), before the mailing date of the first Office Action on the merits.

RELEVANCE OF EACH DOCUMENT

All of the documents are in English.

Applicants respectfully request that each listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 CFR §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 50-0872. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 50-0872.

Respectfully submitted,

Date 3/27/06

By _____

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Substitute for form 1449B/PTO				*Complete if Known*	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				**Application Number**	10/535,042
				Filing Date	05/13/2005
				First Named Inventor	Downes et al.
				Group Art Unit	1646
(use as many sheets as necessary)				Examiner Name	Unknown
Sheet	1	of	5	Attorney Docket Number	SALK3140US-1 (088802-9803)

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	U.S. Patent Document Number	U.S. Patent Document Kind Code[2] (*if known*)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	A1	6184353		Evans	02-06-2001	

U.S. PATENT APPLICATION DOCUMENTS

Examiner Initials*	Cite No.[1]	U.S. Patent Application Document Serial Number	U.S. Patent Application Document Kind Code[2] (*if known*)	Name of Patentee or Applicant of Cited Document	Filing Date of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document Office[3]	Foreign Patent Document Number[4]	Foreign Patent Document Kind Code[5] (*if known*)	Name of Patentee or Applicant of Cited Documents	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T[6]

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	A2	Blumberg and Evans (1998). Orphan nuclear receptors--new ligands and new possibilities. Genes Dev. 12(20), 3149-55.	
	A3	Blumberg et al. (1998). SXR, a novel steroid and xenobiotic-sensing nuclear receptor. Genes Dev. 12(20), 3195-3205.	
	A3	Chiang (2002) Bile Acid regulation of gene expression: roles of nuclear hormone receptors. Endocr Rev. 23(4), 443-463.	

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	A4	Egea et al. (2000). Crystal structure of the human RXRa ligand-binding domain to its natural ligand: 9-cis retinoic acid EMBO J. 19, 2592-2601.	
	A5	Evans RM. (1988) The steroid and thyroid hormone receptor superfamily. Science. 240(4854), 889-895.	
	A6	Forman et al. (1995). Identification of a nuclear receptor that is activated by farnesol metabolites. Cell 81, 687–693.	
	A7	Goodwin et al (2000). A regulatory cascade of the nuclear receptors FXR, SHP-1, and LRH-1 represses bile acid biosynthesis. Mol Cell. 6(3), 517-526.	
	A8	Grober et al., (1999) Identification of a bile acid-responsive element in the human ileal bile acid-binding protein gene. J Biol Chem. 274(42), 29749-54	
	A9	Jez et al. (2000) Dissection of malonyl-coenzyme A decarboxylation from polyketide formation in the reaction mechanism of a plant polyketide synthase. Biochemistry 39, 890-902.	
	A10	Kast et al. (2002). Regulation of multidrug resistance-associated protein 2 (ABCC2) by the nuclear receptors pregnane X receptor, farnesoid X-activated receptor, and constitutive androstane receptor. J Biol Chem. 277(4), 2908-15.	
	A11	Laffitte et al. (2000). Identification of the DNA binding specificity and potential target genes for the farnesoid X-activated receptor. J Biol Chem. 275(14), 10638-47	

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	A12	Lattman, Use of the rotation and translation functions. *Meth. Enzymol.* **115**:55-77 (1985)	
	A13	Makishima et al, (1999) Identification of a nuclear receptor for bile acids. Science. 284(5418), 1362-5	
	A14	McPherson, Crystallization of proteins from polyethylene glycol. *J. Biol. Chem.* **251**:6300-6303 (1976)	
	A15	Nicolaou et al. (2000). Natural product-like combinatorial libraries based on privileged structures. 1. General principles and solid-phase synthesis of benzopyrans. J. Am. Chem. Soc. 122, 9939 – 9953 (2000)	
	A16	Nicolaou et al. (2000). Natural product-like combinatorial libraries based on privileged structures. 2. Construction of a 10 000-membered benzopyran library by directed split-and-pool chemistry using nanoKans and optical encoding. J. Am. Chem. Soc. 122, 9954 – 9967 (2000)	
	A17	Nicolaou et al. (2000). Natural product-like combinatorial libraries based on privileged structures. 3. The "Libraries from Libraries" principle for diversity enhancement of benzopyran libraries. J. Am. Chem. Soc. 122, 9968 – 9976 (2000)	
	A18	Parks et al. (1999). Bile acids: natural ligands for an orphan nuclear receptor. Science. 284(5418). 1365-8	

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				First Named Inventor	Downes et al.
				Group Art Unit	1646
(use as many sheets as necessary)				Examiner Name	Unknown
Sheet	4	of	5	Attorney Docket Number	SALK3140US-1 (088802-9803)

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	A19	Pellicciari et al. (2002). 6-alpha-ethyl-chenodeoxycholic acid (6-ECDCA), a potent and selective FXR agonist endowed with anticholestatic activity. J Med Chem. 45(17), 3569-72	
	A20	Rochel et al. (2000). The Crystal Structure of the Nuclear Receptor for Vitamin D Bound to its Natural Ligand. Mol Cell 5, 173-179	
	A21	Sinal et al. (2000). Targeted disruption of the nuclear receptor FXR/BAR impairs bile acid and lipid homeostasis. Cell: 102(6), 731-44	
	A22	Stehlin et al. (2001). X-ray structure of the orphan nuclear receptor RORbeta ligand-binding domain in the active conformation. EMBO J. 20(21), 5822-31	
	A23	Urizar et al (2000). The farnesoid X-activated receptor mediates bile acid activation of phospholipid transfer protein gene expression. J Biol Chem. 275(50), 39313-7	
	A24	Urizar et al. (2002). A natural product that lowers cholesterol as an antagonist ligand for FXR. Science. 296(5573), 1703-6	
	A25	Wang et al. (1999) Endogenous bile acids are ligands for the nuclear receptor FXR/BAR. Mol Cell. 3(5), 543-53	

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	A26	Watkins et al. (2001). The Human Nuclear Xenobiotic Receptor PXR: Structural Determinants of Directed Promiscuity, Science, 292, 2329-2333	
	A27	Xu et al. (2001). Structural determinants of ligand binding selectivity between the peroxisome proliferator-activated receptors. Proc Natl Acad Sci U S A. 98(24), 13919-24	

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